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Drug-design strategies against viral diseases

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Abstract

The current study deals with the drug design strategies against viruses belong to the vector-borne diseases, mainly Flaviviridae and those which cause viral haemorrhagic fevers (VHFs), including Ebola and Crimean-Congo viruses which have mortality rates up to 90%. Despite a high mortality rate, no licensed antiviral drugs or vaccines are currently available against these viruses. Although phenomenal efforts have been made in recent years in therapeutic advancements. Modern computational drug discovery has proven to accelerate the challenging process at any stage in the preclinical development of drug candidates. The availability of crystal structures for key proteins involved in viral life cycle made it possible to formulate inhibitor design studies. A multi-pronged developed structure and ligand-based drug design approaches were utilized followed by molecular dynamics simulations against Zika-protease and identified one analogue showed promising activity (IC50 = 10 µM) against Zika virus which lacks cytotoxicity (CC50 > 100 µM). Whereas, *in-silico* approaches also identified potential hits against Ebola, Congo virus and recently emerged SARS-CoV-2, which warrant *in-vitro* evaluations. The study was also extended to other viral diseases like HIV, which identified HIV entry inhibitors by targeting co-receptors, including very selective C-C chemokine receptor type 5, CCR5 antagonist (IC50 = 10.6 µM), and dual CCR5/CXCR4 antagonist. The lead compounds identified after hierarchical drug design strategies with potential antiviral activity profile will be further optimized, and the 3D-QSAR model might leads to identify potential compounds with improved specificity and activity.

Biography:

Muhammad Usman Mirza is in final year of his PhD and studying in KU Leuven, Belgium. He is working in the area of drug discovery and medicinal chemistry. He has over 25 publications that have been cited over 280 times (H-index 8), and has been working in collaboration with various research groups around the globe.

Speaker Publications:

1. "Integrated Computational Approach for Virtual Hit Identification against Ebola Viral Proteins VP35 and VP40"; October 2016International Journal of Molecular Sciences 17(11):1748

2." Towards peptide vaccines against Zika virus: Immunoinformatics combined with molecular dynamics simulations to predict antigenic epitopes of Zika viral proteins", December 2016Scientific Reports 6:37313 DOI: 10.1038/srep37313

3. Loss-of-function mutations in ADCY3 cause monogenic severe obesity"; February 2018Nature Genetics 50(2) DOI: 10.1038/s41588-017-0023-6

4. Perspectives towards antiviral drug discovery against Ebola virus; November 2018Journal of Medical Virology DOI: 10.1002/jmv.253

5. Structural Elucidation of SARS-CoV-2 Vital Proteins: Computational Methods Reveal Potential Drug Candidates Against Main Protease, Nsp12 RNA-dependent RNA Polymerase and Nsp13 Helicase; March 2020

19th International Conference on Pharmaceutics & Novel Drug Delivery Systems; Webinar; June 18-19, 2020

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